## REMARKS

The claims have been amended in response to the new ground of rejection set forth in the Decision on Appeal dated May 28, 2004. Claims 1-6 have been amended to exclude therefrom the compounds identified as structures 33 and 34 in Table 1 of the Bergeron reference of record (US 5,962,533). In addition, new claim 8, drawn to antidiarrheal and/or gastrointestinal anti-spasmodic compositions containing compounds of structures 33 and 34 has been added. Inasmuch as no new matter is embodied by the proposed amendments, entry thereof is respectfully requested.

The Board, in its decision, rejected the Examiner's rationale inherent in the final rejection of the claims over Bergeron. In place thereof the Board raised a new ground of rejection stating:

> *"---As set forth in Bergeron '[a]ll of the compounds [of Table 1] were screened for their --- C50values --- Bergeron discloses that to determine 1 C51values, the polyamine derivatives of Table 1 were diluted in sterile water --- In our opinion sterile water is a pharmaceutically acceptable carrier. Thus, Bergeron discloses a composition comprising a compound of formula 1 (see Table 1, compounds 33 and 34) in a pharmaceutically acceptable carrier (sterile water). The question remains, however, as to whether Bergeron teaches a composition comprising an amount of compound 33 or 34 that would meet the requirements of appellant's claimed invention? --- While Bergeron does not teach the amount of the compound in the composition, it appears, absent evidence to the contrary that the composition of claim 1 is identical or substantially identical to the composition disclosed by Bergeron as useful in the determination of IC 50 values. Appellant's burden under the circumstances presented herein was described in In re Best, 195 USPQ 430, 433-434 --- We find no evidence on this record that the composition of Bergeron does not necessarily or inherently possess the characteristics of appellant's claimed composition---".*

It is respectfully submitted that the Board's reasoning, as stated above, is fatally flawed as applied to new claim 8 and claim 7 for two reasons. First, the so-called "compositions" referred to by the Board are not "pharmaceutical compositions" as specified in the rejected claims. The Bergeron "compositions" are merely solutions of the compounds

suitable for screening the compounds for "their 48 and 96 hour $IC_{50}$ values in L1210 cell culture assays" (col. 19, lines 35-38, emphasis added). Applicant is aware of no authority, nor has the Board cited any, for the proposition that a solution suitable for an *in vitro* assay is equivalent to or even suggestive of a pharmaceutical composition. The present claims are drawn to "pharmaceutical compositions suitable for administration to a human or nonhuman animal in need thereof". Nowhere in the reference is there a disclosure or suggestion of such a composition containing either compound 33 or 34. Certainly, the mere disclosure of a "screening solution" useful for an *in vitro* cell culture assay is not tantamount to such a disclosure.

Secondly, the reference discloses no specific amounts of either compound 33 or 34 present in the screening solutions. Thus, the skilled artisan is provided with no insight as to any amount of compound to place in solution, much less an amount effective to achieve an anti-diarrheal effect in a therapeutic setting. It is of course well settled in the law that a reference must enable the practice of a claimed invention before it can be said to disclose or suggest the invention. *In re Legrice*, 133 USPQ 365; *Phillips v. Ladd,* 138 USPQ 421; *Dupont v. Ladd*, 140 USPQ 297; *In re Brown*, 141 USPQ 245; *In re Foster*, 145 USPQ 166; *In re Dow*, 5 USPQ2d 1529.

It is apparent that one skilled in the art would be unable to prepare any composition containing either compound 33 or 34, based on the information contained in Bergeron since no amounts of the compounds are set forth.

Since the present claims specify amounts of the compounds effective to treat diarrhea, for example, and the reference relied upon sets forth no amounts whatsoever, it cannot be said to anticipate the invention. It is, of course, well settled that "a prior art reference must teach one of ordinary skill in the art to make or carry out the claimed invention without

undue experimentation" (*Minnesota Mining and Manufacturing Co. v. Chemique, Inc.* 303 F3d 1294, 64 USPQ2d 1270 (Fed. Cir. 2002)).

In *In re Wands*, 858 F2d 721, 8 USPQ2d 1400 (Fed. Cir. 1998), it is stated that the factual premises of enablement in a prior art reference may include the following:

(1.) the quality of experimentation necessary;

(2.) the amount of direction and guidance given;

(3.) the nature of the invention;

(4.) the state of the prior art;

(5.) the relative skill of those in the art;

(6.) the predictability or unpredictability of the art; and

(7.) the breadth of the claims.

It is readily apparent that the reference relied upon fails on all seven counts to qualify as an enabling disclosure of the claimed invention since no amounts of the critical compounds are set forth. See also In re Grose, 201 USPQ 57, and In re Wiggins, 179 USPQ 421.

Attention is also directed to the decision in *Elan Pharmaceuticals Inc. v. Mayo Foundation for Medical Education and Research*, 68 USPQ2d 1373 (CAFC, Nov., 2003) wherein the CAFC held that the disclosure of an assertedly anticipating prior art reference must be adequate to enable possession of desired subject matter, and a reference that merely names or describes the desired subject matter thus does not anticipate it if the subject matter cannot be produced without undue experimentation, stating:

> *"---To serve as an anticipating reference, the reference must enable that which it is asserted to anticipate.* 'A claimed invention cannot be anticipated by a prior art reference if the allegedly anticipatory disclosures cited as prior art are not enabled.' [Amgen, Inc. v. Hoechst Marion Roussel, Inc,, 314 F.3d 1313, 1354, 65 USPQ2d 1385, 1416 (Fed. Cir. 2003). See Bristol-Myers Squibb v. Ben Venue Laboratories, Inc., 246 F.3d 1368, 1374, 58 USPQ2d 1508, 1512 (Fed. Cir, 2001) ('To anticipate the reference must also enable one of skill in the art to make and use the claimed invention.'); PPG Industries, Inc. v. Guardian Industries Corp., 75 F.3d 1558, 1566, 37

> USPQ2d 1618, 1624 (Fed. Cir. 1996) ('To anticipate a claim, a reference must disclose every element of the challenged claim and enable one skilled in the art to make the anticipating subject matter.') ---*Enablement requires that 'the prior art reference must teach one of ordinary skill in the art to make or carry out the claimed invention without undue experimentation.' [Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d 1362, 1369, 52 USPQ2d 1129, 1134 (Fed. Cir. 1999)* ('Whether undue experimentation would have been required to make and use an invention, and thus whether a disclosure is enabling under 35 U.S.C. § 112, 11, is a question of law that we review de novo, based on underlying factual inquiries that we review for clear error.')]. *(See also) In re Goodman, 29 USPQ2d 2010, 2015 (Fed. Cir, 1993). --- The principles underlying application of the criteria of enablement to the content of the prior art were discussed in In re Donohue, 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985):* 'It is well settled that prior art under 35 U.S.C. § 102(b) must sufficiently describe the claimed invention to have placed the public in possession of it. Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his own knowledge to make the claimed invention. Accordingly, even if the claimed invention is disclosed in a printed publication, that disclosure will not suffice as prior art if it is not enabling. It is not, however, necessary that an invention disclosed in a publication shall have actually been made in order to satisfy the enablement requirement.' Id. at 533, 226 USPQ at 621. *See also In re Borst, 345 F.2d 851, 855, 145 USPQ 554, 557 (CCPA 1962)* ('the disclosure must be such as will give possession of the invention to the person of ordinary skill. Even the act of publication or the fiction of constructive reduction to practice will not suffice if the disclosure does not meet this standard.'). ---*The determination of what level of experimentation is "undue," so as to render a disclosure non-enabling, is made from the view-point of persons experienced in the field of the invention. See Enzo Biochem, supra:* 'The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art.' In re Wands, 8 USPQ2d 14001 (Fed. Cir. 1988). *In Wands the court observed that* '[t]he test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed' quoting In re Jackson, 217 USPQ 804, 817---"

Clearly, the weight of authority supports the proposition that a reference that does not enable one skilled in the art to possess what is allegedly disclosed does not disclose it within the meaning of the patent laws. Since Bergeron does not enable a solution or composition containing either compound 33 or 34, the reference cannot be said to anticipate, either

expressly or inherently, any pharmaceutical composition containing either of the compounds. Stated differently, a nonenabled disclosure cannot be said to anticipate anything.

Attention is also directed to the decision in *In re Gangadharam* 13 USPQ2d 1568 (CAFC, 1989), wherein the court held that the disclosure of *in vitro* test was insufficient on which to reject claims drawn to an *in vivo* utility. What makes that decision extremely relevant to the present fact situation is that in *Gangadharam*, at least the *in vitro* and *in vivo* tests were related; still, the court held that the former did not suggest or anticipate the latter. In the present case, the respective tests are not even remotely related; one being concerned with $IC_{50}$ values in a L1210 cell culture assay and the other to an antidiarrheal pharmaceutical composition. Certainly, if the *in vitro* test in *Gangadharam* was insufficient to anticipate the related *in vivo* utility, the *in vitro* test of the reference is insufficient to anticipate the completely unrelated related *in vivo* utility of the present claims.

Accordingly, withdrawal of this ground of rejection is respectfully requested.

It is clear from the Board's decision that the above-stated new ground of rejection was not intended to apply to claims that did not include compounds 33 or 34 of the Bergeron reference. Thus, the Board went to great lengths to emphasize that dependent claims 2-7 were included in the rejection solely because applicant had stated in his Brief that all of the claims would stand or fall together. Since the rejection is based on 35 USC § 102(b) and the Examiner and Board agreed that compounds 33 and 34 of the reference were the only compounds disclosed that were encompassed by the claims, present claims 1-6, which specifically exclude these two compounds are not subject to rejection over Bergeron under §102(b).

Applicants have earnestly endeavored to place this application in condition for allowance and an early action to that end is respectfully requested.

Respectfully submitted,

Miles & Stockbridge

Dennis P. Clarke
Registration No. 22,549

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DPC/maa

1751 Pinnacle Drive
Suite 500
McLean, Virginia 22102-3833
Telephone: (703) 903-9000
Facsimile: (703) 610-8686
E-mail: dclarke@milesstockbridge.com